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ALCOHOL ALERT

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Alcohol Withdrawal Syndrome

The alcohol withdrawal syndrome is a cluster of symptoms observed in persons who stop drinking alcohol following continuous and heavy consumption. Milder forms of the syndrome include tremulousness, seizures, and hallucinations, typically occurring within 6-48 hours after the last drink. A more serious syndrome, delirium tremens (DTs), involves profound confusion, hallucinations, and severe autonomic nervous system overactivity, typically beginning between 48 and 96 hours after the last drink (Victor 1983). Estimates vary on the incidence of serious consequences of alcohol withdrawal. Regardless of actual incidence, recent evidence suggests that it may be important to treat everyone who is suffering from alcohol withdrawal.

Alcohol Alert, a publication of the National Institute on Alcohol Abuse and Alcoholism, provides timely information on alcohol research and treatment to health professionals and other interested people. This issue is the fifth in the series.

In a classic study that has shaped our understanding of alcohol withdrawal for many years, Isbell et al. (1955) found that alcohol-related seizures occur only after stopping heavy drinking. In a recent study that looked primarily at seizures, Ng et al. (1988) challenged Isbell's concept and reported that the risk of first seizure is related to current alcohol use rather than to withdrawal. They concluded, based on self-reports given retrospectively by seizure patients, that the relationship of alcohol use to seizures is causal and dose-dependent. However, emerging neurophysiological findings lend support to Isbell's interpretation of withdrawal.

Evidence mounts for drug treatment of alcohol withdrawal

In the central nervous system, ethanol (in concentrations high enough to intoxicate humans) interferes with the processes that tell certain nerve cells to activate or become excited (Hoffman et al. 1989; Lovinger et al. 1989). It also enhances those processes that tell certain nerve cells to be restrained (Suzdak et al. 1986). Thus, ethanol acts as a nonspecific biochemical inhibitor of activity in the central nervous system. During withdrawal, a person's central nervous system experiences a reversal of this effect: Excitatory processes are enhanced while inhibitory processes are reduced (Morrow et al. 1988). Such changes can result in overactivation of the central nervous system when alcohol is withdrawn.

Alcohol interferes with CNS processes

Clinical researchers have measured this overactivation in patients (Linnoila et al. 1987). Even patients with moderately severe alcohol withdrawal can experience sympathetic nervous system overactivity and increased production of the adrenal hormones cortisol and norepinephrine. Both of these hormones can be toxic to nerve cells. Moreover, cortisol can specifically damage neurons in the hippocampus (Sapolsky et al. 1986)—a part of the brain that is thought to be particularly important for memory and control of affective states. Thus, repeated untreated alcohol withdrawals may lead to direct damage to the hippocampus.

Ballenger and Post (1978) did a retrospective chart review that led them to postulate that repeated inadequately treated withdrawals could produce future withdrawals of increased severity. These authors suggested that this phenomenon may be analogous to kindling as described in the animal literature. In kin-

Each untreated withdrawal may worsen future withdrawals

A Commentary by NIAAA Director Enoch Gordis, M.D. ***3***

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dling, repeated, weak (subthreshold), electrical or pharmacological stimulation of certain parts of the central nervous system leads to increased sensitivity; an animal eventually exhibits behavioral changes (including seizures) that are more severe on each occasion. The implication is that repeated untreated withdrawals from alcohol have a cumulative effect and create more serious future withdrawals. Only a minority of chronic alcoholics develop a seizure disorder, so an inherited vulnerability may be involved. Many investigators (e.g., Linnoila et al. 1987) now believe that chronic alcoholics who cannot maintain abstinence should receive pharmacotherapy to control withdrawal symptoms, thereby reducing the potential for further seizures and brain damage.

Benzodiazepines are drugs of choice

In a recent review of pharmacological treatments for alcohol intoxication, withdrawal, and dependence, Liskow and Goodwin (1987) concluded that the drugs of choice for treating withdrawal are the benzodiazepines—e.g., the longer-acting benzodiazepines chlordiazepoxide (Librium) and diazepam (Valium) or the shorter-acting benzodiazepines oxazepam (Serax) and lorazepam (Ativan).

"Loading dose" strategy merits consideration

Physicians traditionally have used benzodiazepines by administering decreasing doses over the period of alcohol withdrawal. Rosenbloom (1988) recommends this approach, suggesting the use of intermediate half-life benzodiazepines (such as lorazepam), or even shorter half-life drugs (such as midazolam), because these drugs do not linger in the system and allow for doses to be easily titrated to the patient's response. However, Sellers et al. (1983) introduced a different approach. At the start of treatment, doses of diazepam are given every 1 to 2 hours until withdrawal symptoms abate. Because diazepam has a long half-life and produces a psychoactive metabolite (desmethyldiazepam) with an even longer half-life, there is usually no need for further medication. This strategy, called "loading dose," simplifies treatment, protects against seizures, and eliminates possible reinforcement of drug-seeking behavior in patients who otherwise might receive additional medication for relief of symptoms.

Other agents, such as the beta-blocker propranolol (Sellers et al. 1977), the beta-blocker atenolol in combination with oxazepam (Kraus et al. 1985), and the alpha-2-adrenoreceptor agonist clonidine (Manhem et al. 1985; Robinson et al. 1989), have been tested and shown to alleviate some symptoms of the withdrawal syndrome, but there is no clear evidence of their efficacy in preventing seizures (Liskow and Goodwin 1987). Potential drugs for future use are calcium channel blockers (Koppi et al. 1987) and carbamazepine, which are now in the early stages of evaluation (Butler & Messiha 1986).

Experience with drug-free withdrawal

Most clinicians use medications to diminish the symptoms of alcohol withdrawal. However, Whitfield et al. (1978) reported success with nondrug detoxification of a group of ambulatory patients with uncomplicated alcoholism. The treatment consisted of screening and providing extensive social support during withdrawal. The authors concluded that nondrug detoxification offers a reduced need for medical staff, a shortened detoxification period, and no sedative interference with a patient's alertness for participating in an alcohol treatment program.

Assessment scales are finding clinical use

Several researchers have developed scales for assessing the severity of the alcohol withdrawal syndrome: the Total Severity Assessment and Selected Severity Assessment (Gross et al. 1973), the Abstinence Symptom Evaluation Scale (Knott et al. 1981), and the Clinical Institute Withdrawal Assessment Scale [CIWA] (Shaw et al. 1981). Originally developed as research tools for studying treatment efficacy, such scales are now finding clinical use. Foy et al. (1988) demonstrated that a modified version of the CIWA can assist in guiding treatment and predicting patients at risk for severe alcohol withdrawal. Such scales also may be helpful when monitoring the adequacy of a loading dose of medication. However, rating procedures are not infallible, and an occasional patient will have

a more severe reaction than the scale predicts. Rating procedures cannot replace the clinical judgment of medical staff.

Rating procedures cannot replace clinical judgment

One final point deserves mention. A recent study by Hayashida et al. (1989) compared outpatient with inpatient detoxification. The researchers concluded that outpatient medical detoxification is "an effective, safe, and low-cost treatment for patients with mild-to-moderate symptoms of alcohol withdrawal." However, the data from this study indicate that inpatient detoxification was more effective than outpatient detoxification: At the 6-month followup those treated as inpatients reported significantly greater improvement in their drinking behavior, despite having been measured as more impaired than the outpatient group at the time of admission. This point is not emphasized in the report. Whereas outpatient detoxification may be cheaper for some alcoholics, it is not clear to what extent serious comorbidities, which may be undetected outside a hospital setting, may lead to more severe and expensive problems later.

Alcohol Withdrawal Syndrome — A Commentary by NIAAA Director Enoch Gordis, M.D.

A variety of techniques exist for managing alcohol withdrawal, some that involve pharmacotherapy with sedatives and some that do not. Based on current literature, it appears that it is probably safe to treat mild withdrawal without drugs. However, research on treating alcohol withdrawal is just beginning to accumulate. Recent research findings show a potential for central nervous system damage to patients who experience repeated withdrawals and suggest that all patients exhibiting alcohol withdrawal symptoms receive pharmacotherapy. As evidence increases, it may well be that pharmacotherapy becomes the recommended choice in all withdrawal cases. Therefore, it is vital that clinicians keep abreast of the literature to ensure that their patients receive the most up-to-date care.

When using sedatives to treat alcohol withdrawal, understanding the relative advantages and disadvantages of different drug administration techniques is important. Administering an initial dose of a long-acting benzodiazepine, like diazepam, with repeated doses every 2 hours until symptoms subside, then stopping the drug, simplifies treatment and frees patients and staff to focus on the recovery process, not drug dosage schedules. However, this method could cause problems if sedation is found to complicate an existing medical condition, such as chronic obstructive pulmonary disease, because the drugs, or their metabolites, remain in the body for several days. On the other hand, by giving repeated doses of a short-acting benzodiazepine (e.g., oxazepam), probably for several days, if complications to medical conditions are found, the drugs can be easily stopped due to their rapid elimination by the body. But this regimen is less easily managed because medication must be given around the clock, and it could result in the patient and staff attending to the drug-taking regimen rather than to recovery.

In deciding which drug administration technique to use for individual patients, there is no substitute for a thorough medical evaluation. There is a welcome trend toward using the CIWA and other clinical scales for measuring withdrawal syndrome severity and for guiding drug treatment decisions; their use should be encouraged. However, no scaling instrument is infallible. Withdrawal severity scales should be used to complement, not replace, a thorough clinical evaluation of the patient's medical status.

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